



Complete Summary

GUIDELINE TITLE

Guidelines on the management of Waldenström macroglobulinaemia.

BIBLIOGRAPHIC SOURCE(S)

Johnson SA, Birchall J, Luckie C, Oscier DG, Owen RG, Haemato-Oncology Task Force of the British Committee for Standards in Haematology. Guidelines on the management of Waldenstrom macroglobulinaemia. Br J Haematol 2006 Mar;132(6):683-97. [108 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [December 18, 2006 - Rituxan \(Rituximab\)](#): Health care professionals informed about important emerging safety information regarding the development of progressive multifocal leukoencephalopathy (PML) in patients under treatment with Rituxan.

COMPLETE SUMMARY CONTENT

**** REGULATORY ALERT ****

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis

RECOMMENDATIONS

EVIDENCE SUPPORTING THE RECOMMENDATIONS

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

QUALIFYING STATEMENTS

IMPLEMENTATION OF THE GUIDELINE

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY

DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Waldenström's macroglobulinaemia

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Hematology
Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide guidelines for the management and treatment of patients with Waldenström's macroglobulinaemia

TARGET POPULATION

Patients with Waldenström's macroglobulinaemia

INTERVENTIONS AND PRACTICES CONSIDERED

1. Plasma exchange
2. Alkylating agent-based therapy
3. Purine analogues (fludarabine, cladribine)
4. Other therapies
 - Rituximab
 - Thalidomide
5. High-dose therapy with autologous stem-cell transplantation

MAJOR OUTCOMES CONSIDERED

- Response to therapy
- Adverse effects
- Quality of life
- Survival

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The PubMed which contains MEDLINE (1951-date), Cochrane Library and EMBASE (1974- date) databases in English language was searched using the key words "Waldenstrom's Macroglobulinaemia/Waldenstrom's Macroglobulinemia/macroglobulinaemia,/macroglobulinemia further refined by the sub-searches plasmapheresis/plasma exchange. Database searches were augmented by checking reference lists of useful articles identified. No language or publication restrictions were applied. Where important preliminary data exists only in abstract form this has been included but preference has been given throughout to peer-reviewed publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomised controlled trials

Ib Evidence obtained from at least one randomised controlled trial

IIa Evidence obtained from at least one well designed controlled study without randomisation

IIb Evidence obtained from at least one other type of well designed quasi-experimental study

III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The recommendations were drawn up using the methods outlined in the AGREE instrument (<http://www.agreecollaboration.org>).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendations

Grade A

Evidence level Ia and Ib

Required – at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing specific recommendation

Grade B

Evidence levels IIa, IIb, and III

Required – availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation.

Grade C

Evidence level IV

Required – evidence obtained from expert committee reports or opinions and/or clinical experiences of respects authorities. Indicates absence of directly applicable clinical studies of good quality

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The recommendations were reviewed by a Sounding Board of 80 haematologists representing adult practice in both teaching and district hospitals.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (**I–IV**) and strength of evidence (**A–C**) supporting the recommendations are defined at the end of the "Major Recommendations" field.

Plasma Exchange

- 1-2 procedures, exchanging 1-1½ calculated plasma volumes is advised for the treatment of hyperviscosity syndrome (HVS) in Waldenström's macroglobulinaemia (WM). In patients who are drug resistant this may be indicated as long term management. **Level of evidence III, Grade of recommendation B.**

Neuropathies

- The evidence supporting plasma exchange for the treatment of peripheral neuropathy associated with an IgM paraprotein is weak. **Level of evidence III-IV, Grade of recommendation C.**

Cryoglobulinaemia

- Although there are few studies, which consider the role of plasma exchange in the treatment of cryoglobulinaemia, there is a clear rationale for its use. **Level of evidence III-IV, Grade of recommendation C.** The treatment room should be warm and blood warmers used in the cell separator circuit to prevent precipitation during the procedure.

Combination Chemotherapy

- Alkylating-agent based therapy is appropriate for the initial and subsequent treatment of Waldenström's Macroglobulinaemia. **Level of evidence IIa, Grade of recommendation B.**

Purine Analogues

- Purine analogues are appropriate for the initial and subsequent treatment of Waldenström's Macroglobulinaemia. There is no consensus on the duration of treatment with cladribine or fludarabine, or on which purine analogue is superior. **Level of Evidence IIa, Recommendation B.** Fludarabine is more active than cyclophosphamide, doxorubicin and prednisolone (CAP) as salvage therapy, **Level of Evidence Ib, Grade of recommendation A.**

Other Treatments

- Rituximab is active in the treatment of WM but associated with the risk of transient exacerbation of clinical effects of the disease and should only be used with caution especially in patients with symptoms of hyperviscosity and/or IgM levels > 40g/L. **Level of evidence IIb, Grade of recommendation B.**
- Thalidomide is of potential use in the treatment of patients who have previously received alkylating agents, purine analogues and antibody therapy. Other agents are currently only recommended in the context of clinical trials. **Level of evidence III, Grade of recommendation B.**

High Dose Therapy

- High dose therapy supported by autologous stem-cell transplantation has a role in the management of selected patients with WM with primary refractory or relapsed disease. **Level of evidence III, Grade of recommendation B.**

Definitions:

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomised controlled trials

Ib Evidence obtained from at least one randomised controlled trial

IIa Evidence obtained from at least one well designed controlled study without randomisation

IIb Evidence obtained from at least one other type of well designed quasi-experimental study

III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

Grades of Recommendations

Grade A

Evidence level Ia and Ib

Required – at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing specific recommendation

Grade B

Evidence levels IIa, IIb, and III

Required – availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation.

Grade C

Evidence level IV

Required – evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of Waldenström's macroglobulinaemia, including control of disease, prevention of complications, improved quality of life, and prolonged survival

POTENTIAL HARMS

- Side effects of plasma exchange, chemotherapy and conditioning therapy for stem cell transplantation, and immune therapies
- Treatment-related mortality

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

While the advice and information in these guidelines is believed to be true and accurate at the time of going to press, neither the authors, the British Society for Haematology nor the publishers accept any legal responsibility for the content of these guidelines.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005

GUIDELINE DEVELOPER(S)

British Committee for Standards in Haematology - Professional Association

SOURCE(S) OF FUNDING

British Committee for Standards in Haematology

GUIDELINE COMMITTEE

Haemato-Oncology Task Force

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: SA Johnson, Taunton and Somerset Hospital; J Birchall, National Blood Service, Bristol; C Luckie, D Oscier, Royal Bournemouth Hospital; RG Owen, HMDS, Leeds

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

SAJ has received support to travel to meetings and fees for speaking at satellite symposia from Schering and Roche and has served on the advisory boards of Schering, Roche and Janssen-Cilag. RGO has received support to attend meetings and fees for lectures and organising educational events from Roche and support for research from Roche, Amgen and Schering. DGO has received support to attend meetings from Schering and Roche. The WM1 trial is supported by an unrestricted grant from Schering Healthcare.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [British Committee for Standards in Haematology Web site](#).

Print copies: Available from BCSH Secretary, British Society for Haematology, 100 White Lion Street, London N1 9PF; E-mail: jules@b-s-h.org.uk

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on September 26, 2006. The information was verified by the guideline developer on October 25, 2006. This summary was updated by ECRI on January 12, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Rituxan (Rituximab).

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